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TITLE: TREATMENT OF ADULT SEVERE TRAUMATIC BRAIN INJURY USING AUTOLOGOUS BONE MARROW MONONUCLEAR CELLS

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14. ABSTRACT
Traumatic brain injury (TBI) contributes to 50% of all trauma deaths. The mortality rate for adults following severe TBI (Glasgow Coma Scale < 9) is estimated to be 33%. There is currently no therapy to reverse the primary injury associated with TBI. Over the past 10 years there has been a growing body of literature supporting the use of various progenitor cell types to treat acute neurological injuries such as TBI. Our primary hypothesis is that bone marrow mononuclear cell (BMMNC) autologous transplantation after TBI is safe (harvest and infusion related toxicity) after TBI. Our secondary hypothesis is that functional outcomes measures will improve after BMMNC infusion, (3) BMMNC infusion will reduce BBB permeability, and (4) BMMNC is neuroprotective and preserves grey matter and white matter volumes after TBI. Patients, ages18 to 55 years old, admitted to Memorial Hermann Hospital Trauma Center with Glasgow Coma Scores (GCS) of 5 to 8 are screened. This is a dose-escalation study consisting of 4 cohorts including a control group (5 subjects/cohort). The first five subjects will not undergo the bone marrow harvest procedure; though they will be followed and treated the same as the other study participants and complete all follow-up procedures. Subjects are followed for safety, have plasma and CSF (if available) collected for neuroinflammatory markers, and at 30-days and 6 months post-injury, neuropsych and functional outcomes testing and DTMRI are performed. To date, 3 subjects have been enrolled (all controls) and have had plasma collected for neuroinflammatory markers and have returned for their 30-day follow-up visits. Per protocol, all charts were reviewed by the medical monitor and there have been no serious adverse events to report.

15. SUBJECT TERMS
Traumatic Brain Injury, Bone Marrow Mononuclear Cells

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TREATMENT OF ADULT SEVERE TRAUMATIC BRAIN INJURY USING AUTOLGOUS BONE MARROW MONONUCLEAR CELLS

Annual Progress Report (01-June-2011 to 31-May-2012)

Introduction:
Traumatic brain injury (TBI) contributes to 50% of all trauma deaths. The mortality rate for adults following severe TBI (Glasgow Coma Scale < 9) is estimated to be 33%. There is currently no therapy to reverse the primary injury associated with TBI. Over the past 10 years there has been a growing body of literature supporting the use of various progenitor cell types to treat acute neurological injuries such as TBI and stroke. Neural stem cells (adult and embryonic), mesenchymal stromal and multipotent adult progenitor cells, and bone marrow mononuclear cells (from which MSC and MAPCs are derived) have all shown efficacy in pre-clinical models of TBI/stroke through various mechanisms; however, few groups believe that true neural replacement and integration are the putative mechanisms involved in the observed efficacy. More likely is that the progenitor cell populations are modifying the regional response to injury (inflammatory/reparative vs. regenerative), resulting in improved functional outcomes. Our primary hypothesis is that bone marrow mononuclear cell (BMMNC) autologous transplantation after TBI is safe (harvest and infusion related toxicity) after TBI. Our secondary hypothesis is that functional outcomes measures will improve after BMMNC infusion, (3) BMMNC infusion will reduce BBB permeability and (4) BMMNC is neuroprotective and preserves grey matter and white matter volumes after TBI.

Body:
Patients, ages18 to 55 years old, admitted to Memorial Hermann Hospital Trauma Center with Glasgow Coma Scores (GCS) of 5 to 8 are screened. Those patients meeting inclusion/exclusion criteria (or their Legal Authorized Representative [LAR]) are offered consent to participate by the investigator. This is a dose-escalation study consisting of 4 cohorts including a control group (5 subjects/cohort). The first five subjects will not undergo the bone marrow harvest procedure (3 of the 5 enrolled to date); though they will be followed and treated the same as the other study participants and complete all follow-up procedures. Subjects 6-10 will receive the lowest dose target of $6X10^6$ mononuclear cells/kilogram body weight. Subjects 11-15 will receive $9x10^6$ mononuclear cells/kilogram body weight, and lastly Subjects 16-20 will receive $12X10^6$ mononuclear cells/kilogram body weight. All subjects will be followed for safety, have plasma and CSF (if available) collected for neuroinflammatory markers, and will return at 30-days and 6 months post-injury for neuropsych and functional outcomes testing and DTMRI.

Key Research Accomplishments:
The FDA approved this protocol under IND 12620 on April 20, 2011.

Final approval from the University of Texas Health Science Center at Houston Committee for the Protection of Human Subjects was received on October 19, 2011.

Approval from the Army HRPO was received on December 20, 2011.

Recruitment was open on March 1, 2012.

To date, 3 subjects have been enrolled (all controls) and have had plasma collected for neuroinflammatory markers and have returned for their 30-day follow-up visits. Per the protocol, all charts were reviewed by the medical monitor and there have been no serious adverse events to report.

Reportable Outcomes:

N/A - There are no outcomes to report at this time as this project just began enrolling two months ago.

Conclusion:

N/A

References:

N/A

Appendices:

N/A